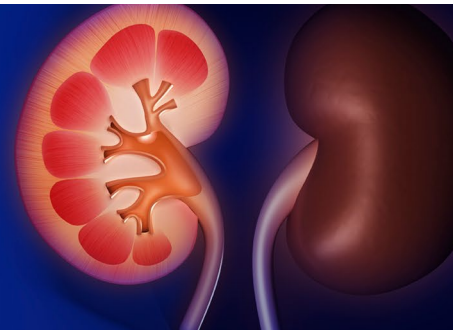


Nephrology Practice Review™



Making Education Easy

Issue 3 - 2019

In this issue:

- > ADA: Diabetic nephropathy recommendations
- > Presymptomatic screening for intracranial aneurysms in ADPKD
- > EAU guideline on RCC
- > EAU guideline on RCC: Immune checkpoint inhibition
- > Renal transplant vitamin D recommendations challenged
- > Reducing intestinal phosphorus load in CKD
- > Long term outcomes in monoclonal gammopathy of renal significance
- > Renal hyperfiltration: A risk factor for CVD and mortality
- > The use of ESAs in patients with CKD and cancer
- > Familial kidney cancer: New syndromes and molecular insights
- > Potassium additives in hyperkalaemia management
- > Conferences, workshops and CPD

Abbreviations used in this issue:

ADA = American Diabetes Association;
ADPKD = autosomal dominant polycystic kidney disease;
CKD = chronic kidney disease; **EAU** = European Association of Urology;
eGFR = estimated glomerular filtration rate;
ESA = erythropoiesis-stimulating agent; **ESRD** = end-stage renal disease;
MRGS = monoclonal gammopathy of renal significance;
RCC = renal cell carcinoma; **SGLT2** = sodium-glucose cotransporter 2;
TKI = tyrosine kinase inhibitor.

Claim CPD/CME points [Click here](#) for more info.

Follow RESEARCH REVIEW Australia on Twitter now

 @ResearchRevAus
Visit <https://twitter.com/ResearchRevAus>

Welcome to the third issue of Nephrology Practice Review.

This new Review covers news and issues relevant to clinical practice in nephrology. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally, on the back cover you will find a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this new Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne

Medical Research Advisor

janette.tenne@researchreview.com.au

Clinical Practice

ADA: Diabetic nephropathy recommendations

The American Diabetes Association (ADA) has made important changes to its 2019 Standards of Care based on findings from the CRENDENCE (Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy) trial, which were published in April in the *New England Journal of Medicine*.

In CRENDENCE, 4401 patients with diabetic nephropathy were randomised to receive the sodium-glucose cotransporter 2 (SGLT2) inhibitor canagliflozin or placebo. Interim results showed that patients on canagliflozin had a 30% lower risk of the composite endpoint of end-stage renal disease (ESRD), doubling of serum creatinine, or death from renal or cardiovascular causes.

Updated recommendations include:

- Assess urinary albumin (e.g., spot urinary albumin-to-creatinine ratio) and estimated glomerular filtration rate at least once a year in all patients with type 2 diabetes, in patients with type 1 diabetes with duration of 5 or more years and in all patients with comorbid hypertension.
- Consider use of a SGLT2 inhibitor in patients with type 2 diabetes and diabetic nephropathy who have an eGFR of 30 mL/min/1.73 m² or higher and particularly in patients with albuminuria exceeding 300 mg/g to reduce the risk of CKD progression and cardiovascular events.
- Consider use of a glucagon-like peptide 1 receptor agonist to reduce the risk of albuminuria progression and cardiovascular events in patients with CKD who are at increased risk for cardiovascular events.
- The previous recommendation for microvascular complications and foot care (recommendation 11.8) has been removed based on findings from CRENDENCE.

According to ADA, the risk-benefit profile of SGLT2 inhibitor treatment appears favourable for most patients with type 2 diabetes and CKD. An increased risk for diabetic ketoacidosis was noted with canagliflozin, but no increased risks for lower-limb amputations, fractures, acute kidney injury, or hyperkalaemia.

Download the update [here](#).

Kindly Supported by



PBS
1ST JAN
2019

Help protect the kidneys Help change the outlook for patients¹⁻⁵

Advancing
the treatment
of ADPKD^{1,2,5}



PLEASE REVIEW PRODUCT INFORMATION BEFORE PRESCRIBING. CLICK HERE.

1. Torres VE et al. *N Engl J Med*. 2012;367(25):2407-18.
2. Torres VE et al. *N Engl J Med*. 2017;377(20):1930-42
3. Gansevoort RT, et al. *Nephrol Dial Transplant*. 2016;31(3):337-48.
4. JINARC Product Information
5. Australian Public Assessment Report for Tolvaptan, February 2018; <https://www.tga.gov.au/auspar/auspar-tolvaptan-0>.



Presymptomatic screening for intracranial aneurysms in patients with ADPKD

In patients with autosomal dominant polycystic kidney disease (ADPKD), screening for brain aneurysms may identify hidden lesions, although knowing that a patient has an aneurysm does not change their management or affect screening recommendations, a review from the Mayo Clinic suggests.

ADPKD is characterized by progressive development of bilateral kidney cysts and extrarenal abnormalities including intracranial aneurysms. The authors of the review found that brain aneurysms were detected during presymptomatic screening in 9% of patients with ADPKD, and more frequently in those with a history of hypertension and smoking. Very few patients experienced aneurysmal ruptures, but the overall rupture rate was approximately five times higher than in the general population.

The authors approach has been to recommend screening for patients with ADPKD who have a family history of aneurysm. They also recommend screening to patients with ADPKD before major elective surgeries, those with occupations where rupture would place the lives of others at risk, and those who after being properly informed on the available data wish to be screened for reassurance.

Study details

The study reviewed medical records of 3010 patients with ADPKD who were evaluated at the Mayo Clinic. A total of 812 patients underwent presymptomatic brain screening; an aneurysm was detected in 9% of these patients.

During a mean follow-up of 9 years, none of the 94 intracranial aneurysms detected by presymptomatic screening ruptured. The aneurysm was repaired in 7 patients. Risk factors for intracranial aneurysm were identified. Thirty-seven percent of patients with an aneurysm on brain screening had a family history of either intracranial aneurysm or subarachnoid haemorrhage, compared to 18% of those who had no aneurysm detected. Patients with intracranial aneurysm were also more likely to have hypertension and a history of smoking than those who did not have an aneurysm. During a mean follow-up of 8 years, de novo aneurysms were detected in five patients in whom an aneurysm had been previously detected. None of these aneurysms ruptured.

Among patients with no evidence of an aneurysm on initial screening who underwent additional testing, three developed an aneurysm during the follow-up period; two patients had a rupture. Both patients had significant risk factors for brain aneurysm development and rupture. The overall rupture rate in the ADPKD patients was approximately five times higher than in the general population.

[Clin J Am Soc Nephrol. 2019 Aug 7;14\(8\):1151-1160.](#)

[Media release.](#)

EAU guideline on renal cell carcinoma

The European Association of Urology (EAU) has updated its guideline for renal cell carcinoma (RCC) based on new data. The guideline was first published in 2000. The 2019 guideline presents a limited update of the 2018 publication. Updated recommendations are discussed below.

Recommendations for the management of other renal tumours

There is a strong recommendation to treat Bosniak type IV cysts the same as RCC. There are only weak recommendations to treat Bosniak type III cysts the same as RCC or offer cautious surveillance, and offer active surveillance to patients with biopsy-proven oncocytomas, as an acceptable alternative to surgery or ablation.

Recommendations for adjuvant therapy

New evidence shows that, after nephrectomy in selected high-risk patients, adjuvant sunitinib improves disease-free survival, but not overall survival. However, adjuvant sorafenib, pazopanib or axitinib does not improve disease-free survival or overall survival after nephrectomy. Therefore, there is now a strong recommendation to not offer adjuvant therapy with sorafenib, pazopanib or axitinib.

Recommendations for local therapy of advanced/metastatic RCC

New evidence shows that cytoreductive nephrectomy followed by sunitinib is non-inferior to sunitinib alone in patients with metastatic clear-cell RCC. In addition, sunitinib alone is non-inferior compared to immediate cytoreductive nephrectomy followed by sunitinib in patients with MSKCC intermediate- and poor-risk RCC who require systemic therapy with a VEGFR-tyrosine kinase inhibitor (TKI). Accordingly, there is now a strong recommendation to not offer cytoreductive nephrectomy in MSKCC poor-risk patients.

Weak recommendations are as follows:

- Do not perform immediate cytoreductive nephrectomy in MSKCC intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy with a VEGFR-TKI, but rather, start systemic therapy. In such patients who attain long-term sustained benefit and/or minimal residual metastatic burden, discuss delayed cytoreductive nephrectomy.
- Perform immediate cytoreductive nephrectomy in patients with good performance who do not require systemic therapy, and in patients with oligometastases when complete local treatment of the metastases can be achieved.

[Eur Urol. 2019 May;75\(5\):799-810.](#)

EAU guideline on renal cell carcinoma: Immune checkpoint inhibition

Recent randomised trials have shown a survival benefit for a front-line ipilimumab and nivolumab combination therapy, and pembrolizumab and axitinib combination therapy in metastatic clear-cell RCC. The EAU has updated its recommendations based on these studies.

For patients with International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) intermediate- and poor-risk disease, axitinib/pembrolizumab or nivolumab/ipilimumab should now be considered the standard of care. For patients with favourable-risk disease, axitinib/pembrolizumab is recommended.

Among patients who cannot receive or tolerate immune checkpoint inhibitors, sunitinib and pazopanib are recommended for those with IMDC favourable-risk disease, and, for patients with intermediate- or poor-risk disease, sunitinib, pazopanib and cabozantinib are recommended.

Regarding later-line therapy, after immune oncology, any VEGF-targeted therapy that has not been used previously in combination with immune oncology is recommended. After axitinib/pembrolizumab, changing the VEGFR-TKI at progression is recommended, which may be cabozantinib or any other TKI not previously used.

[Eur Urol. 2019 Aug;76\(2\):151-156.](#)

Renal transplant vitamin D recommendations challenged

Higher doses of vitamin D than are currently recommended in guidelines may be necessary to reduce fracture risk in renal transplant recipients, according to a study presented at the 56th European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Congress in Budapest, Hungary, in June.

KDIGO (Kidney Disease: Improving Global Outcome) guidelines recommend correction of vitamin D deficiency to improve bone health based on guidelines for the general population, but high-grade evidence supporting this recommendation is not available.

In a prospective, multicentre, double-blind controlled trial, 536 kidney transplant recipients received vitamin D (cholecalciferol) either 12,000 IU (low dose) or 100,000 IU (high dose) every 2 weeks for 2 months, then monthly for 22 months. The low dose was equivalent to the minimum recommended intake of 400 IU per day.

At two years, vitamin D levels were significantly higher in the high-dose group (43.1 ng/mL vs 25.1 ng/mL in the low-dose group). The incidence of fractures was significantly lower in the high-dose group (1% vs 4% in the low-dose group). There were no between-group differences in the risks of diabetes, major cardiac events, new cancers, or death. High-dose vitamin D was well tolerated, with no increased risks of vascular calcification, hypercalcaemia or hyperphosphatemia.

The authors concluded that that currently recommended doses of vitamin D are not high enough to protect patients from the risk of fracture after kidney transplantation.

[Media release.](#)

The role of phosphate-containing medications and low dietary phosphorus-protein ratio in reducing intestinal phosphorus load in patients with chronic kidney disease

A review published in *Nutrition and Diabetes* highlights the role of phosphate-containing medications and foods with a low phosphorus-to-protein ratio in reducing intestinal phosphorus load in patients with CKD.

Many drugs commonly prescribed to CKD patients contain phosphorus. However, the amount of phosphate in a specific drug varies widely. For example, amlodipine 10 mg for a dialysis patient contains anywhere from 7.9 to 165.6 mg of available phosphorus, depending on the manufacturer. More than 20% of medications in the following categories contain phosphate as an excipient: calcium channel blockers (51%); pain medicines (45%); antipsychotics (35%); vitamins (29%); diabetes drugs (24%); beta blockers (23%); cholesterol-lowering therapy (21%).

Both pharmaceutical excipients and food additives have inorganic phosphates that are readily absorbed from the intestine. The estimated amount of phosphorus in medications in 90% of the patients with CKD may be <80 mg/day, which is much lower than the phosphorus concentration from food additives, which may be as high as 800 mg/day. Nevertheless, medicinal drugs as a hidden source of phosphorus in patients with CKD cannot be overlooked.

The reviewers recommend vigilant prescription of phosphate-containing medications and consideration of alternative drugs to decrease intestinal phosphorus load.

The review also highlights use of the dietary phosphate (mg) to protein (g) ratio to select foods for an optimal CKD diet. The estimated phosphorus load from 1 g of protein is 13 to 15 mg, of which 30% to 70% is intestinally absorbed. Low phosphorus foods (e.g., egg white) have a phosphorus-protein ratio of less than 12 mg/g.

[Nutr Diabetes. 2019 Apr 3;9\(1\):14.](#)



News in brief

Long term outcomes in monoclonal gammopathy of renal significance

The long-term outcomes of patients with monoclonal gammopathy of renal significance (MGRS) is unclear. This paper reviewed the outcomes of 41 patients with biopsy-confirmed MGRS treated in five centres across the UK and Ireland. Thirty-three patients (80.5%) were kappa light chain restricted and 27 patients (65.9%) had light chain deposition disease. Estimated renal survival was 81.6% at 24 months and estimated overall survival was 80.3% at 48 months. Patients with CKD stage 2-3b at diagnosis had an estimated renal survival of 100% at 24 months, compared to 80.7% in patients with CKD stage 4-5 (P = 0.04). Delayed diagnosis due to small plasma cell clones and requirement for renal biopsy were associated with poorer outcomes.

[Br J Haematol. 2019 May 29. doi: 10.1111/bjh.15987.](#)

Renal hyperfiltration defined by high estimated glomerular filtration rate: A risk factor for cardiovascular disease and mortality

Renal hyperfiltration, that is, increased glomerular filtration rate above normal values, is associated with early phases of kidney disease in patients with obesity and diabetes. Although glomerular hyperfiltration is a risk factor for the progression of CKD, the consequences of renal hyperfiltration as a risk factor for cardiovascular disease and mortality are not well understood. Recent evidence in a number of settings, including healthy individuals and patients with diabetes or established cardiovascular disease, suggests that renal hyperfiltration is associated with a higher risk of cardiovascular disease and all-cause mortality. In this review, the authors summarize the existing evidence, discuss possible mechanisms, and describe the remaining knowledge gaps regarding the association of renal hyperfiltration with risk of cardiovascular disease and mortality.

[Diabetes Obes Metab. 2019 Jul 12. doi: 10.1111/dom.13831.](#)

The use of erythropoiesis-stimulating agents in patients with CKD and cancer

This paper offers an overview of a clinical approach to the use of erythropoiesis-stimulating agents (ESAs) in patients with CKD and cancer. Usually, clinicians try to maintain haemoglobin (Hb) levels in the 10 to 11 g/dL range because of the absence of objective benefit of normalizing Hb levels and increased evidence of ESA-induced complications in patients with anaemia. In 2000, the US Food and Drug Association changed oncology guidelines regarding ESA use for chemotherapy-induced anaemia because of associations of ESAs with increased mortality, thrombotic complications, and cerebrovascular accidents. However, no guidance was provided for patients with CKD and cancer. The lowest ESA doses possible that achieve a maximum Hb level of 10 g/dL have been recommended by these authors for individuals with CKD and cancer. There is a lack of data showing an increased probability of occurrence of new cancers in relation to the use of ESAs in patients on dialysis or earlier stages of CKD.

[Am J Kidney Dis. 2019 Aug 5. pii: S0272-6386\(19\)30767-X.](#)

Familial kidney cancer: Implications of new syndromes and molecular insights

Hereditary cases make up 5% of all cases of RCC. With advances in next-generation sequencing, several new hereditary syndromes have been described recently. This review discusses the diagnosis and management of familial kidney cancer syndromes. It describes updates in testing and management of the most common syndromes such as von Hippel-Lindau, and hereditary leiomyomatosis and RCC, along with insights into recently described familial kidney cancer syndromes.

[Eur Urol. 2019 Jul 17. pii: S0302-2838\(19\)30500-7.](#)

Potassium additives and bioavailability: Are we missing something in hyperkalaemia management?

Hyperkalaemia is a common metabolic disturbance in CKD. Management may include instructions on adhering to a low-potassium diet. Use of potassium additives in processed foods is growing and its bioavailability exceeds that of potassium in whole foods. Teaching patients with CKD about potassium additives and a low potassium diet has become as important as teaching them about phosphorus.

[J Ren Nutr. 2019 Jul;29\(4\):350-353.](#)

RESEARCH REVIEW™ Australia's Leader in Specialist Publications



JINARC is the first and only treatment approved for slowing the progression of Autosomal Dominant Polycystic Kidney Disease (ADPKD).^{1,2}

Advancing
the treatment
of ADPKD³⁻⁵



PLEASE REVIEW PRODUCT INFORMATION BEFORE PRESCRIBING. [CLICK HERE.](#)

1. Australian Public Assessment Report for Tolvaptan, February 2018; <https://www.tga.gov.au/auspar/auspar-tolvaptan-0>. 2. Sans-Atxer L, Joly D. *Int J Nephrol and Renovasc Dis.* 2018;11:41-51. 3. Torres VE et al. *N Engl J Med.* 2012;367(25):2407-18. 4. Torres VE et al. *N Engl J Med.* 2017;377(20):1930-42. 5. JINARC Product Information



Conferences, Workshops and CPD

Please click on the links below for upcoming local and international nephrology meetings, workshops and CPD.

[ANZSN - Upcoming Conferences and Meetings](#)

[Renal Society of Australasia - Events](#)

[TheConferenceWebsite – Renal Medicine Conferences](#)

[Conferenceseries.com – Nephrology Conferences](#)

[COMS - Conferences and Meetings on Nephrology](#)

[The Transforming Role of the Perioperative Nurse 27 October - 3 November 2019](#)

Contact

Research Review™

Email geoff@researchreview.com.au Phone 1300 132 322

Research Review publications

Nephrology Research Review

with Professor Vlado Perkovic

<https://tinyurl.com/y8tuowwg>

Renal Cancer Research Review

with Dr Craig Gedge

<https://tinyurl.com/y6yxtrhy>

Product Review - Tolvaptan in the management of autosomal dominant polycystic kidney disease

<https://tinyurl.com/y2mmx8cn>

Product Review - Nivolumab plus ipilimumab for advanced renal cell carcinoma

<https://tinyurl.com/yxv8lxk9>

Study Review - Characterisation of patients with metastatic renal cell carcinoma

<https://tinyurl.com/y3sojked>

RESEARCH REVIEW™ Australia's Leader in Specialist Publications

PBS eligibility criteria¹

1. ≥18 years of age and
2. CKD stage 2 or 3 (eGFR 89 to 30 mL/min/1.73m²) at initiation of treatment and
3. Evidence of rapid progression determined by:
 - eGFR decline of ≥5 mL/min/1.73m² in one year or
 - eGFR decline of ≥2.5 mL/min/1.73m² per year over a period of 5 years

Phone 1800 059 606 or email oapmedical@au.otsuka.com

Get certified now at JINARC.com.au



Advancing
the treatment
of ADPKD²⁻⁴

JINARC®
tolvaptan

PBS Information: Authority required. Refer to PBS Schedule for full authority information.

PLEASE REVIEW PRODUCT INFORMATION BEFORE PRESCRIBING. CLICK HERE.

1. The Pharmaceutical Benefits Scheme, <http://www.pbs.gov.au/medicine/item/11588X-11593E-11596H-11597J-11600M-11602P> 2. Torres VE et al. *N Engl J Med.* 2012;367(25):2407-18. 3. Torres VE et al. *N Engl J Med.* 2017;377(20):1930-42 4. JINARC Product Information. JINARC® is a registered trademark of Otsuka Pharmaceutical Co., Ltd. Otsuka Australia Pharmaceutical Pty Ltd, ABN 20 601 768 754. Chatswood NSW 2067. December 2018. JIN-1812-102.01



Australian Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our [CPD page](#).

Practice Reviews cover news and issues relevant to Australian clinical practice.

Research Review Australia Pty Ltd is an independent Australian publisher. Research Review receives funding from a variety of sources including Government depts., health product companies, insurers and other organisations with an interest in health. Journal content is created independently of sponsor companies with assistance from leading local specialists. **Privacy Policy:** Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time. **Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits. To contact Research Review Australia, please email geoff@researchreview.com.au.

Research Review publications are intended for Australian health professionals.

